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10/781,318	02/18/2004	Daniel J. Conklin	961094.00030	9433

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EXAMINER

KWON, BRIAN YONG S

ART UNIT	PAPER NUMBER
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1614

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/781,318	Applicant(s) CONKLIN, DANIEL J.	
	Examiner Brian S. Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 November 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above claim(s) 6-8 and 13-53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 9-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants Response to Restriction Requirement Acknowledged

1. Applicant's election, with traverse, with the Group II(a) claims along with methylamine as the elected species is acknowledged.

Applicants traverse the restriction requirement on the grounds that there would be no burden in searching the entire groups. This argument is not persuasive, as claimed invention would be distinctive, each from the other for the reason of the record. Furthermore, the search of the entire groups in the non-patent literature (a significant part of a thorough examination) would be burdensome. Therefore, the requirement is still deemed proper, and made Final. Claims 6-8 and 13-53 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

2. Claims 1-5 and 9-12 are currently pending for prosecution on the merits.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1614

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-5 and 9-12 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claims are drawn to a method of processing (Merriam-Webster dictionary defines "process" as "a series of actions or operations conducing to an end; *especially* : a continuous operation or treatment especially in manufacture") a blood vessel, comprising preparing a blood vessel for implantation in a patient and exposing the blood vessel to a physiologically acceptable solution containing an exogenous substrate for an SSAO enzyme.

The instant specification discloses that the SSAO substrates are converted by SSAO into products that, in turn, cause vasorelaxation, which is useful for treating various diseases and conditions, including high blood pressure and vasospasm, including those observed in surgical treatments wherein a donor blood vessel is to be implanted into a patient. For instance, the donor blood vessels can be bathed in solution containing an exogenous substrate for an SSAO enzyme (see page 2, line 7 through page 3, line 5).

The specification discloses a method of vasodilating a blood vessel in a patient undergoing a surgical blood vessel implantation comprising exposing the blood vessel to a physiological solution that comprises an exogenous substrate for an SSAO enzyme, which meets the written description. However, claim 1 fails to provide sufficient written description to support to the instantly claimed method of making blood vessel. A process of making blood

Art Unit: 1614

vessel having physiological and biology entity is totally different from a process of dilating blood vessel. The skilled artisan cannot envision the instant invention based upon the provided disclosure.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF’s were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art

Art Unit: 1614

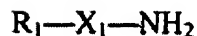
to recognize that [the inventor] invented what is claimed.”) Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of vasodilating a blood vessel in a patient undergoing a surgical blood vessel implantation comprising preparing a blood vessel taken from a donor patient and exposing the blood vessel to a physiological solution that comprises an exogenous substrate for an SSAO enzyme represented by a chemical formula



or

, does not reasonably provide enablement

for “a method of processing a blood vessel...an exogenous substrate for an SSAO enzyme”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Art Unit: 1614

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant claims are drawn to a method for processing a blood vessel, comprising preparing a blood vessel for implantation in a patient and exposing the blood vessel to physiologically acceptable solution that comprises an exogenous substrate for an SSAO enzyme.

With respect to enable of "an exogenous substrate for an SSAO enzyme",

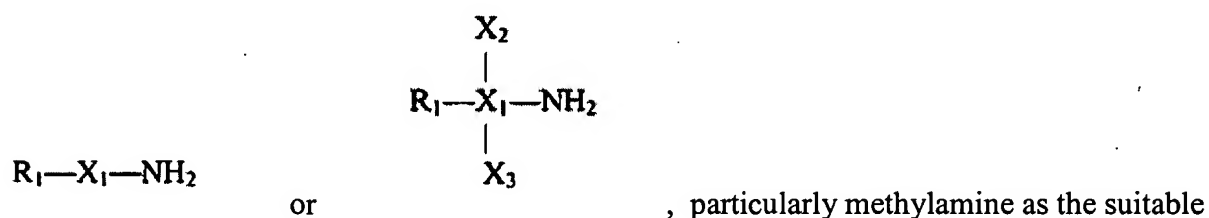
The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive

Art Unit: 1614

dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5(BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotrophic hormones was unpredictable art; In re Wright, 999 F.2d 1577, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of the “exogenous substrate for an SSAO enzyme” prior to filling of the instant invention was an unpredictable art.

The claims are very broad due to the vast number of possible compounds of that are described as being “exogenous substrate for an SSAO enzyme”. The instant claims cover “exogenous substrate for an SSAO enzyme” that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

Although the specification discloses compounds of the formula



“exogenous substrate for an SSAO enzyme”, the specification fails to provide how to make/screen “exogenous substrate for an SSAO enzyme” without undue amount of experimentation. As discussed in preceding comments, in the instant case, only a limited number of compounds that are structurally similar to methylamine which is represented by the formula are set forth, thereby failing to provide sufficient working examples. It is noted that these

Art Unit: 1614

examples are neither exhaustive, nor define the class of compounds required. The instant claims read on any compounds having “exogenous substrate for an SSAO enzyme”, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fishcher, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575.

As discussed above, considering above factors, especially the “sufficient working examples”, “the level of skill in the art”, “the relative skill and the unpredictability in the pharmaceutical art”, “breadth of the claims” and “the chemical nature of the invention”, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds for the claimed methods of prevention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claim 1-3, 5 and 9 are rejected under 35 U.S.C. 102(a) as being anticipated by Vidrio et al. (The Journal of Pharmacology and Experimental Therapeutics, Vol. 307:497-504, 2003).

Vidrio discloses that SSAO substrates such as benzylamine, phenethylamine and methylamine potentiate vasodilation activity of hydralazine. (abstract; 'Experiments in Rat Aortic Rings'; 'Discussion'). Vidrio discloses experimental study involving preparing blood vessel (aortic ring) pretreated methylamine (400 mg/kg, i.p.).

7. Claim 1-5 and 9-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Nipro Corporation (EP 1459763 A1).

EP'763 teaches a use of a composition comprising alpha2-macroglobulin inactivating compound such as methylamine, ethylamine for the treatment of vascular restenosis, wherein said composition is delivered to blood vessel during the coronary intervention via an implantable intravascular device; and wherein said compound is present at the narrowed area of the blood vessel in ranges from 1 to 100 mM (abstract; para. [0040] and [0042] and claim 9).

Art Unit: 1614

Claim Rejections - 35 USC § 103

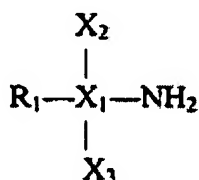
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
8. Claims 1-5 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldstein et al. (US 7129035) and further in view of Seamonds et al. (The Journal of Biological Chemistry, Vol. 246, No. 17, pp.5391-5397, 1971).

Goldstein teaches a method of sterilizing or preserving organ or living tissues for later implantation by providing implantable tissue product (e.g., blood vessels, arteries, veins, heart valves, tendons, ligaments) and exposing said product to an aqueous solution comprising bio-compatible buffer such as tris(hydroxymethyl)aminomethane (which read on the compound of



the formula

) buffered solution, wherein said bio-compatible buffer has

Art Unit: 1614

a concentration of from 20 to 75 mM in said aqueous solution; and wherein said buffered solution maintains the pH of said aqueous solution from about 7 to 8 (see abstract; column 5, lines 38-52; column 6, lines 8-42; claims). However, the claimed invention fails to teach use of methylamine and the specific osmolarity.

However, one having ordinary skill in the art would have been motivated to select methylamine (known buffering agent as taught by Seamonds, see 'Summary') with the expectation that methylamine would not significantly alter the analogous properties of the compound of the reference (tris(hydroxyethyl)aminomethane) due to close structural similarity of the compounds.

With respect to the specific osmolarity, generally differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Conclusion

9. No Claim is allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Art Unit: 1614

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov> Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
Primary Patent Examiner
AU 1614

A handwritten signature in dark ink, appearing to read 'B. Kwon', followed by a long horizontal line extending to the right.